

CLAIMS

I claim:

1. An isolated polypeptide, comprising at least 15 contiguous amino acid residues of an amino acid sequence of SEQ ID NO:38 or SEQ ID NO:48 selected from the group consisting of:

- (a) amino acid residues 24 to 230;
- (b) amino acid residues 27 to 230;
- (c) amino acid residues 27 to 126; and
- (d) amino acid residues 131 to 230.

2. The isolated polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO:38 or SEQ ID NO:48 selected from the group consisting of:

- (a) amino acid residues 24 to 230;
- (b) amino acid residues 27 to 230;
- (c) amino acid residues 27 to 126; and
- (d) amino acid residues 131 to 230.

3. The isolated polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence of SEQ ID NO:38 or SEQ ID NO:48 selected from the group consisting of:

- (a) amino acid residues 24 to 230;
- (b) amino acid residues 27 to 230;
- (c) amino acid residues 27 to 126; and
- (d) amino acid residues 131 to 230.

4. An isolated polypeptide, comprising an amino acid sequence that is at least 90% identical to a reference amino acid sequence of SEQ ID NO:38 or SEQ ID NO:48 selected from the group consisting of:

- (a) amino acid residues 24 to 230;

- (b) amino acid residues 27 to 230;
- (c) amino acid residues 27 to 126; and
- (d) amino acid residues 131 to 230.

5. The isolated polypeptide of claim 4, wherein the isolated polypeptide comprises an amino acid sequence of SEQ ID NO:38 or SEQ ID NO:48 selected from the group consisting of:

- (a) amino acid residues 24 to 230;
- (b) amino acid residues 27 to 230;
- (c) amino acid residues 27 to 126; and
- (d) amino acid residues 131 to 230.

6. An isolated nucleic acid molecule, wherein the nucleic acid molecule is either (a) a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:39 or SEQ ID NO:49, or (b) a nucleic acid molecule that remains hybridized following stringent wash conditions to a nucleic acid molecule consisting of the nucleotide sequence of nucleotides 8 to 697 or 77 to 697 or 86 to 697 of SEQ ID NO:37 or SEQ ID NO:47, or the complement of the nucleotide sequence of nucleotides 8 to 697 or 77 to 697 or 86 to 697 of SEQ ID NO:37 or SEQ ID NO:47.

7. The isolated nucleic acid molecule of claim 6, wherein any difference between the amino acid sequence encoded by the nucleic acid molecule and the corresponding amino acid sequence of SEQ ID NO:38 or SEQ ID NO:48 is due to a conservative amino acid substitution.

8. The isolated nucleic acid molecule of claim 6, comprising the nucleotide sequence of nucleotides 8 to 697 or 77 to 697 or 86 to 697 of SEQ ID NO:37 or SEQ ID NO:47.

9. A vector, comprising the isolated nucleic acid molecule of claim 8.

10. An expression vector, comprising the isolated nucleic acid molecule of claim 8, a transcription promoter, and a transcription terminator, wherein the promoter is operably linked with the nucleic acid molecule, and wherein the nucleic acid molecule is operably linked with the transcription terminator.

11. A recombinant host cell comprising the expression vector of claim 10, wherein the host cell is selected from the group consisting of bacterium, yeast cell, fungal cell, insect cell, mammalian cell, and plant cell.

12. A method of producing mouse Zcytor16 protein, the method comprising culturing recombinant host cells that comprise the expression vector of claim 10, and that produce the mouse Zcytor16 protein.

13. The method of claim 12, further comprising isolating the mouse Zcytor16 protein from the cultured recombinant host cells.

14. An antibody or antibody fragment that binds with the polypeptide of claim 3.

15. The antibody of claim 14, wherein the antibody is selected from the group consisting of: (a) polyclonal antibody, (b) murine monoclonal antibody, (c) humanized antibody derived from (b), and (d) human monoclonal antibody.

16. An anti-idiotypic antibody that specifically binds with the antibody of claim 14.

17. A fusion protein, comprising the polypeptide of claim 3.

18. The fusion protein of claim 17, wherein the fusion protein further comprises an immunoglobulin moiety.

19. An isolated polynucleotide that encodes a soluble cytokine receptor polypeptide comprising a sequence of amino acid residues that is at least 90% identical to the amino acid sequence as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230; and

wherein amino acid differences consist of conservative amino acid substitutions; and

wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide sequence binds IL-TIF or antagonizes IL-TIF activity.

20. An isolated polynucleotide according to claim 19, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a homodimeric, heterodimeric or multimeric receptor complex.

21. An Isolated polynucleotide according to claim 20, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex further comprising a soluble Class I or Class II cytokine receptor.

22. An isolated polynucleotide according to claim 20, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

23. An isolated polynucleotide that encodes a soluble cytokine receptor polypeptide comprising a sequence of amino acid residues as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a homodimeric, heterodimeric or multimeric receptor complex.

24. An Isolated polynucleotide according to claim 23, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide further comprises a soluble Class I or Class II cytokine receptor.

25. An isolated polynucleotide according to claim 23, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

26. An isolated polynucleotide according to claim 23, wherein the soluble cytokine receptor polypeptide further encodes an intracellular domain.

27. An isolated polynucleotide according to claim 23, wherein the soluble cytokine receptor polypeptide further comprises an affinity tag.

28. An expression vector comprising the following operably linked elements:

(a) a transcription promoter; a first DNA segment encoding a soluble cytokine receptor polypeptide having an amino acid sequence as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230; and a transcription terminator; and

(b) a second transcription promoter; a second DNA segment encoding a soluble Class I or Class II cytokine receptor polypeptide; and a transcription terminator; and

wherein the first and second DNA segments are contained within a single expression vector or are contained within independent expression vectors.

29. An expression vector according to claim 28, further comprising a secretory signal sequence operably linked to the first and second DNA segments.

30. An expression vector according to claim 28, wherein the second DNA segment encodes a polypeptide comprising a soluble CRF2-4 receptor polypeptide (SEQ ID

NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

31. A cultured cell comprising an expression vector according to claim 28, wherein the cell expresses the polypeptides encoded by the DNA segments.

32. A cultured cell comprising an expression vector according to claim 28, wherein the first and second DNA segments are located on independent expression vectors and are co-transfected into the cell, and cell expresses the polypeptides encoded by the DNA segments.

33. A cultured cell into which has been introduced an expression vector according to claim 28, wherein the cell expresses a heterodimeric or multimeric soluble receptor polypeptide encoded by the DNA segments.

34. A cell according to claim 31, wherein the cell secretes a soluble cytokine receptor polypeptide heterodimer or multimeric complex.

35. A cell according to claim 31, wherein the cell secretes a soluble cytokine receptor polypeptide heterodimer or multimeric complex that binds IL-TIF or antagonizes IL-TIF activity.

36. A DNA construct encoding a fusion protein comprising:

a first DNA segment encoding a polypeptide having a sequence of amino acid residues as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230; and

at least one other DNA segment encoding a soluble Class I or Class II cytokine receptor polypeptide,

wherein the first and other DNA segments are connected in-frame; and

wherein the first and other DNA segments encode the fusion protein.

37. A DNA construct encoding a fusion protein according to claim 36, wherein at least one other DNA segment encodes a polypeptide comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

38. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA construct encoding a fusion protein according to claim 36; and

a transcription terminator,

wherein the promoter is operably linked to the DNA construct, and the DNA construct is operably linked to the transcription terminator.

39. A cultured cell comprising an expression vector according to claim 38, wherein the cell expresses a polypeptide encoded by the DNA construct.

40. A method of producing a fusion protein comprising:

culturing a cell according to claim 39; and

isolating the polypeptide produced by the cell.

41. An isolated soluble cytokine receptor polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230, and

wherein the soluble cytokine receptor polypeptide binds IL-TIF or antagonizes IL-TIF activity.

42. An isolated polypeptide according to claim 41, wherein the soluble cytokine receptor polypeptide forms a homodimeric, heterodimeric or multimeric receptor complex.

43. An isolated polypeptide according to claim 42, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble Class I or Class II cytokine receptor.

44. An isolated polypeptide according to claim 42, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

45. An isolated soluble cytokine receptor polypeptide comprising a sequence of amino acid residues as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230, wherein the soluble cytokine receptor polypeptide forms a homodimeric, heterodimeric or multimeric receptor complex.

46. An isolated polypeptide according to claim 45, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble Class I or Class II cytokine receptor.

47. An isolated polypeptide according to claim 45, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

48. An isolated polypeptide according to claim 45, wherein the soluble cytokine receptor polypeptide further comprises an affinity tag, chemical moiety, toxin, or label.

49. An isolated heterodimeric or multimeric soluble receptor complex comprising soluble receptor subunits, wherein at least one of the soluble receptor subunits comprises a soluble cytokine receptor polypeptide comprising a sequence of amino acid

residues as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230.

50. An isolated heterodimeric or multimeric soluble receptor complex according to claim 49, further comprising a soluble Class I or Class II cytokine receptor polypeptide.

51. An isolated heterodimeric or multimeric soluble receptor complex according to claim 49, further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35), a soluble IL-10 receptor polypeptide (SEQ ID NO:36), or soluble zcytor11 receptor polypeptide (SEQ ID NO:34).

52. A method of producing a soluble cytokine receptor polypeptide that forms a heterodimeric or multimeric complex comprising:

culturing a cell according to claim 31; and

isolating the soluble receptor polypeptides produced by the cell.

53. A method of producing an antibody to soluble cytokine receptor polypeptide comprising:

inoculating an animal with a soluble cytokine receptor polypeptide selected from the group consisting of:

(a) a polypeptide comprising a monomeric or homodimeric soluble cytokine receptor comprising a polypeptide as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230;

(b) a polypeptide of (a) further comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble Class I or Class II cytokine receptor polypeptide;

(c) a polypeptide of (a) further comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:35);

(d) a polypeptide of (a) further comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble IL-10 receptor polypeptide (SEQ ID NO:36); and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

54. An antibody produced by the method of claim 53, which specifically binds to a homodimeric, heterodimeric or multimeric receptor complex comprising a polypeptide as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230.

55. The antibody of claim 54, wherein the antibody is a monoclonal antibody.

56. An antibody which specifically binds to a homodimeric, heterodimeric or multimeric receptor complex according to claim 49.

57. A method for inhibiting IL-TIF-induced proliferation or differentiation of hematopoietic cells and hematopoietic cell progenitors comprising culturing bone marrow or peripheral blood cells with a composition comprising an amount of soluble cytokine receptor polypeptide as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230, sufficient to reduce proliferation or differentiation of the hematopoietic cells in the bone marrow or peripheral blood cells as compared to bone marrow or peripheral blood cells cultured in the absence of soluble cytokine receptor.

58. The method of claim 57, wherein the hematopoietic cells and hematopoietic progenitor cells are lymphoid cells.

59. The method of claim 58, wherein the lymphoid cells are macrophages or T cells.

60. A method of reducing IL-TIF-induced or IL-9 induced inflammation comprising administering to a mammal with inflammation an amount of a composition of a polypeptide as shown in SEQ ID NO:38 or SEQ ID NO:48 from amino acid 24 to 230, or 27 to 230 sufficient to reduce inflammation.

61. A method of suppressing an inflammatory response in a mammal with inflammation comprising:

- (1) determining a level of serum amyloid A protein;
- (2) administering a composition comprising a soluble mouse Zcytor16 cytokine receptor polypeptide according to claim 41 in an acceptable pharmaceutical vehicle;
- (3) determining a post administration level of serum amyloid A protein;
- (4) comparing the level of serum amyloid A protein in step (1) to the level of serum amyloid A protein in step (3), wherein a lack of increase or a decrease in serum amyloid A protein level is indicative of suppressing an inflammatory response.

62. A method for detecting a cancer in a patient, comprising:

obtaining a tissue or biological sample from a patient;
incubating the tissue or biological sample with an antibody of claim 14 under conditions wherein the antibody binds to its complementary polypeptide in the tissue or biological sample;

visualizing the antibody bound in the tissue or biological sample; and

comparing levels of antibody bound in the tissue or biological sample from the patient to a normal control tissue or biological sample,

wherein an increase in the level of antibody bound to the patient tissue or biological sample relative to the normal control tissue or biological sample is indicative of a cancer in the patient.

63. A method for detecting a cancer in a patient, comprising:

obtaining a tissue or biological sample from a patient;

labeling a polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:37 or SEQ ID NO:47 or the complement of SEQ ID NO:37 or SEQ ID NO:47;

incubating the tissue or biological sample with under conditions wherein the polynucleotide will hybridize to complementary polynucleotide sequence;

visualizing the labeled polynucleotide in the tissue or biological sample; and

comparing the level of labeled polynucleotide hybridization in the tissue or biological sample from the patient to a normal control tissue or biological sample,

wherein an increase in the labeled polynucleotide hybridization to the patient tissue or biological sample relative to the normal control tissue or biological sample is indicative of a cancer in the patient.

64. A transgenic mouse, wherein the mouse over-expresses residues 1 to 230 or 24 to 230, or 27 to 230 of SEQ ID NO:38 or SEQ ID NO:48.

65. A transgenic mouse according to claim 64, wherein the expression of residues 1 to 230 or 24 to 230, or 27 to 230 of SEQ ID NO:38 or SEQ ID NO:48 is expressed using a tissue-specific or tissue-restricted promoter.

66. A transgenic mouse according to claim 64, wherein the expression of residues 1 to 230 or 24 to 230, or 27 to 230 of SEQ ID NO:38 or SEQ ID NO:48 is expressed using an epithelial-specific, colon-specific, or ovary-specific promoter.

67. A transgenic mouse according to claim 64, wherein the mouse does not expresses residues 1 to 230 or 24 to 230, or 27 to 230 of SEQ ID NO:38 or SEQ ID NO:48, relative to a normal mouse.